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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
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TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36030
δ-DODECALACTONE
STUDY NO. 51-0849-77
MARCH 1976 - APRIL 1977

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US ARMY
ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MD 21010

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Photochemical Skin Irritation

(Delta-Dodecalactone)

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A preliminary hazard evaluation of AI3-36030 was performed by means of laboratory animal studies using rats, rabbits and guinea pigs. The technical grade compound did not produce eye or skin irritation or photochmical irritation in rabbits and did not sensitize guinea pigs. Data indicated little acute toxic hazard from accidental ingestion. It was recommended that AI3-36030 be approved for further testing as a candidate insect repellent.

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U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
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δ-DODECALACTONE
STUDY NO. 51-0849-77
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A preliminary hazard evaluation of AI3-36030 was performed by means of laboratory animal studies using rats, rabbits and guinea pigs. The technical grade compound did not produce eye or skin irritation or photochemical irritation in rabbits and did not sensitize guinea pigs. Data indicated little acute toxic hazard from accidental ingestion. It was recommended that AI3-36030 be approved for further testing as a candidate insect repellent.

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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT AI3-36030 δ-DODECALACTONE

STUDY NO. 51-0849-77
MARCH 1976 - APRIL 1977

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 11 March 1976.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the US Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, effective December 1970 with Amendment No. 1, effective August 1974.

2. REFERENCE. Toxicology Division Procedural Guide, USAEHA, 1972.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-36030.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36030, δ-dodecalactone, was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley, Wistar-derived rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:*†

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* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 74-23, revised 1972 - second printing 1974.
† The experiments reported herein were performed in animal facilities, fully accredited by the American Association for Accreditation of Laboratory Animal Care.

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TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits. 0.5 ml technical grade compound applied to each of six rabbits.	Compound AI3-36030 produced no primary irritation of the intact skin and to the skin surrounding an abrasion.	USAEHA Category I (ref Appendix).
EYE IRRITATION STUDIES		
Rabbits		
Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.	Compound AI3-36030 did not produce any injury to the cornea, and, in addition, no injury to the conjunctiva in six out of six rabbits	USAEHA Category A (ref Appendix).
APPROXIMATE LETHAL DOSE (ALD)		
Oral		
Rats (male) - no diluent.	ALD= 2200 mg/kg However, dosage 2200 and above did produce involuntary muscle movement.	Presents little lethal hazard from acute accidental ingestion.

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TEST	RESULTS	INTERPRETATION
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
A single application (0.05 ml) of a 25 percent (w/v) solution of the compound (AI3-36030) and of a 10 percent (w/v) oil of Bergamot solution (positive control) in 95 percent ethyl alcohol, were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.	A 25-percent solution of AI3-36030 in ethanol did not cause a photochemical irritation reaction under test conditions. Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	Compound AI3-36030 did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irriation in humans.
Control		
Following UV exposure of the rabbits 0.05 ml of test compound, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation reactions at 24, 48 and 72 hours.		

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TEST	RESULTS	INTERPRETATION
SENSITIZATION STUDIES		
Guinea Pigs (Male)		
Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36030 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs received and challenged with a 0.1 percent solution of AI3-36030.	Challenge dose of test compound (last intradermal injection) did not produce a *sensitization* reaction.	Compound AI3-36030 did not produce a sensitization reaction under these test conditions and is not expected to produce a sensitization reaction in man.
Ten positive control guinea pigs received and challenged with 0.1 percent suspension of DNCB.	Positive control (DNCB) produced a marked sensitization reaction in ten out of ten guinea pigs.	
Ten cage control guinea pigs.	Cage control guinea pigs showed no greater reaction to test compound and DNCB than were seen in original test groups.	
Five receiving challenge dose of test compound without prior sensitizing doses.		
Five receiving challenge dose of DNCB without prior sensitizing doses.		

* A known skin sensitizer.

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5. CONCLUSION. Technical grade compound did not cause adverse eye, skin effects in rabbits, did not sensitize guinea pigs and prevents little lethal hazard from acute accidental ingestion.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (reference para 1b), it is recommended that AI3-36030, δ-dodecalactone, be approved for further testing as a candidate insect repellent.

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APPENDIX

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals. prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.